ABSTRACT

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Title of Thesis: Study of platinum cytotoxic drug interactions with ABCG2 membrane transporter

Platinum cytotoxic drugs pertain among most frequently used cytotoxic drugs. However, their usage is complicated with development of resistance which can be caused by few mechanisms. The aim of this study is to evaluate possible interactions of cisplatin, carboplatin and oxaliplatin with ABCG2 membrane efflux transporter which causes resistance to many cytotoxic drugs. Hoechst 33342 assay was performed on cell lines MDCKII (parent cell line) and MDCKII-ABCG2 (cell line genetically modified for expression of human ABCG2 gene). Intracellular concentration of Hoechst 33342 was not increased in presence of any tested cytotoxic drug; significant change of Hoechst 33342 intracellular fluorescence was observed only in presence of ABCG2 control substrate mitoxantron and ABCG2 inhibitor fumitremorgin C. Final results did not demostrate interactions of ABCG2 with any studied platinum cytotoxic. It shows insignificant interaction between ABCG2 and platinum cytotoxic drugs and so improbable effect of this transporter on toxicity reduction and development of resistance in clinical use of these compounds.